

EXHIBIT G



American Society of
Health-System Pharmacists®



Drug Shortages Summit

November 5, 2010

Summary Report

The Drug Shortages Summit was co-convened by the American Society of Health-System Pharmacists (ASHP), the American Society of Anesthesiologists (ASA), the American Society of Clinical Oncology (ASCO), and the Institute for Safe Medication Practices (ISMP) on November 5, 2010 in Bethesda, Maryland. The goals of the summit were to:

- Discuss the scope and causes of drug shortages;
- Shed light on the harm to patients that is occurring due to drug shortages;
- Discuss the potential need for changes in public policy and stakeholder practices to prevent patient harm from shortages; and
- Develop an assertive action plan that reflects the recommendations and intent of stakeholders to work together to stop patient harm and disruptions in patient care caused by drug shortages.

Summit participants included representatives from health professional organizations, pharmaceutical manufacturers, and supply chain entities. Representatives of the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention also attended portions of the meeting as observers. A complete list of attendees is found in Appendix A.

This summary report reflects discussion at the Drug Shortages Summit, including recommended actions that will be further evaluated and implemented, if appropriate, based on an assessment of feasibility, impact, and resources required for implementation. Compliance with legal requirements (e.g., Federal Trade Commission regulations) and avoidance of unintended consequences (e.g., hoarding,

ASHP REPORT

ASHP Guidelines on Managing Drug Product Shortages in Hospitals and Health Systems

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Purpose

Drug product shortages can adversely affect drug therapy, compromise or delay medical procedures, and result in medication errors.^{1,2} Health care professionals are increasingly concerned about the clinical effect that shortages have on patients and the tremendous resources required to address shortages.³⁻⁵ Adverse patient outcomes related to drug product shortages^{1,2,6-9} have prompted aggressive management strategies by health care providers and gained the attention of the Joint

Commission,¹⁰ the government,^{11,12} and the media.^{13,14} Drug product shortages adversely affect health-system finances by increasing the cost of delivering patient care, largely through higher drug acquisition and personnel costs.⁶ In addition, shortages create a high level of frustration for everyone involved, including purchasing agents, pharmacists, nurses, physicians, and patients.⁷

Managing drug product shortages is particularly complex for practitioners in hospitals and health systems (hereinafter, "health systems"),

because these facilities routinely treat patients with acute or emergent conditions, use a significant number of medically necessary or single-source products, and use high-cost new drug technologies. These health care providers are challenged during drug product shortages to ensure the provision of seamless, safe, and therapeutically equivalent drug therapy, preferably at comparable costs. The pharmacy department must take a leadership role in efforts to develop and implement appropriate strategies and processes for inform-

Developed through the ASHP Council on Pharmacy Management and approved by the ASHP Board of Directors on January 15, 2009. These guidelines supersede the ASHP Guidelines on Managing Drug Product Shortages dated March 28, 2001.

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ing practitioners of shortages and ensuring the safe and effective use of therapeutic alternatives. Strategic planning is required for managing drug product shortages, just as it is for disasters such as major weather events and mass-casualty incidents.

Because a thorough understanding of why drug product shortages occur is essential for their successful management, these guidelines begin with a description of factors that contribute to or exacerbate shortages. The guidelines then describe a three-phase approach to contingency planning for management of drug product shortages and include strategies for prevention. Given the differences and complexities in health-system organizational arrangements and practice settings, some aspects of these guidelines may not be applicable in all settings. Pharmacy managers should use their professional judgment in assessing and adapting these guidelines to meet their needs.

Contributing factors

For the purpose of these guidelines, a drug product shortage is defined as a supply issue that affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent. Shortages can be the result of one or a combination of factors throughout the supply chain. The supply chain includes sources of raw materials, manufacturers, regulators, wholesalers or distributors, prime vendors, group purchasing organizations, and end-user health care systems. The factors that follow contribute to disruptions in the availability of drug products.

Raw and bulk material unavailability. Disruptions in the supply of raw or bulk materials are especially problematic when the primary or sole source experiences production difficulties or discontinues production, affecting multiple manufacturers. An estimated 80% of the raw materials used in pharmaceuticals comes from

outside the United States.⁴ Availability problems can arise when armed conflict or political upheaval disrupts trade, animal diseases contaminate tissue from which raw materials are extracted, climatic and other environmental conditions depress the growth of plants used to produce raw materials, or raw materials are degraded or contaminated during harvesting, storage, or transport.

Manufacturing difficulties and regulatory issues. Drug product shortages can also occur when the primary or sole manufacturer of a drug product halts or delays production in response to a Food and Drug Administration (FDA) enforcement action concerning noncompliance with current good manufacturing practices (cGMPs). Contributing factors may include antiquated manufacturing equipment, a shift of resources from maintenance of equipment and facilities to research and development, loss of manufacturer personnel experienced in production and compliance issues as a result of company mergers or retirements, cGMP-related problems with subcontractors who supply products to multiple pharmaceutical manufacturers, and limited FDA resources for timely inspections of manufacturing sites.⁴ Resolution of these issues is often a lengthy process and may include inspections to ascertain cGMP compliance, issuance of an injunction against the manufacturer, or seizure of products. In some instances, a manufacturer's decision to close a specific manufacturing facility results in unintended drug product shortages. Such was the case when the sole source for hyaluronidase production closed, leaving no supplier.⁵

FDA enforcement actions are intended to protect the public from potentially unsafe drug products. These actions are evaluated by FDA's Center for Drug Evaluation and Research (CDER) drug shortage coordinator to determine if the action might cre-

ate a shortage of a medically necessary drug product.¹² (FDA's definition of a medically necessary product is discussed in the "Government intervention" section below.) In the event that a significant corrective action involves a medically necessary product, FDA will help the manufacturer return to compliance, consider qualifying additional manufacturing sites, or, in extreme circumstances, permit importation of the product from a foreign manufacturing source once the required quality controls are met.

Voluntary recalls. Voluntary recalls, generally related to manufacturing problems, can cause shortages, especially when a sole manufacturer's drug product dominates the market supply. Voluntary recalls are generally temporary and occur as a result of a minor lapse in manufacturing procedures that would not be subject to FDA legal action. Recalls usually affect specific lots and are conducted either because of a lack of assurance that the recalled product is safe or for reasons not related to safety, such as technical deficiencies in the drug's labeling. An ethical dilemma could arise when it is predictable that complying with the voluntary recall may cause a drug product shortage in a given health system.

Change in product formulation or manufacturer. Changes in a product's formulation or manufacturer may also delay product availability. One example is the transition from albuterol metered-dose inhalers (MDIs) containing chlorofluorocarbons to MDIs containing hydrofluoroalkanes in 2006.

Manufacturers' production decisions and economics. Manufacturers' business decisions are based on a variety of factors, including availability of generic products, market size, patent expiration, drug-approval status, regulatory compliance requirements, and anticipated clinical demand. Occasionally, manufacturers temporarily or permanently reduce production

quantities of certain drug products as they shift production efforts or reallocate resources to other products. A manufacturer's reasoned, sound business decision to discontinue production of a drug product because of insufficient financial return or a high cost to correct manufacturing issues can cause an unanticipated, serious shortage, especially in the instance of a sole-source or medically necessary product.¹⁵ For example, a shortage of diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed was precipitated when one of the manufacturers, claiming low revenues, discontinued its product in 2000.⁵ Manufacturers are not required to notify FDA of a drug discontinuation unless the product is a sole-source or medically necessary product.¹⁶ For medically necessary drugs, FDA can encourage other manufacturers to produce the product or request that the manufacturer not suspend production until an alternative source is available. However, FDA does not have the authority to require a company to make any product, even if it is medically necessary. Even with advance notice, some agents, such as vaccines or antibiotics, are complex to manufacture, and shortages may result even if other manufacturers are willing and able to produce the product. Similarly, business decisions on the part of wholesale distributors and end-user health systems may contribute to drug product shortages.

Industry consolidations. Manufacturer mergers often result in decisions to narrow the focus of product lines or move a production line to a new facility, resulting in the discontinuation or delayed availability of drug products. Mergers between two companies that manufacture similar product lines typically result in single-source products. As the number of manufacturers of a product decreases, resiliency in the supply chain also decreases, making product supplies more vulnerable. Many vac-

cines in the United States are single-source products, in part because of discontinuations and consolidations.

Restricted drug product distribution and allocation. Most hospitals and health systems obtain the majority of their drug products through wholesale distributors. Restricted distribution methods that bypass the normal supply chain can also create shortages. As the result of either market approval requirements or postmarketing surveillance, manufacturers limit the availability of specific drug products. Only selected suppliers and end users who comply with manufacturer agreements can obtain the product. A manufacturer can also place restrictions on available limited supplies, requiring health systems to order directly from the manufacturer or through a specialty distributor to receive an allocation.

Inventory practices. Communication and transportation efficiencies throughout the supply chain have allowed inventory reductions at all levels. Most manufacturers, distribution centers, and health systems use "just-in-time" inventory management to reduce the cost of inventory on hand and optimize cash flow. This strategy is recognized as sound business management for all stakeholders, but an unexpected shortage at any point in the supply chain can significantly affect the end user and patient. Some manufacturers and distributors use inventory management strategies that minimize end-of-quarter or end-of-year product inventories or limit shipments based on yearly quotas.

Poor ordering practices, stockpiling before price increases, hoarding caused by rumors of an impending shortage, and unexpected delivery delays may affect inventory levels in individual health systems. Hospitals in rural areas face additional inventory challenges caused by distant distribution centers and the inability to easily borrow an item from a nearby

hospital. Drug product shortages may also occur when all hospitals in an area disproportionately use the same wholesaler. Some shortages are wholesaler dependent, as shortages of drugs can occur when contracts with suppliers are delayed.

Unexpected increases in demand and shifts in clinical practice. Occasionally, the demand for a drug product unexpectedly increases or exceeds production capacity. This may occur when a new indication is approved for an existing drug product, when usage patterns change in response to new therapeutic guidelines, when a substantial disease outbreak occurs, or when unpredictable factors influence demand. Shortages may be prolonged when the raw materials are limited or manufacturing processes are complex or dependent on a long lead time. For example, when the Centers for Disease Control and Prevention (CDC) recommended annual influenza vaccination for children age 6–59 months in 2006, only one product had FDA-approved labeling for use in children 6–23 months.^{17,18}

Nontraditional distributors. The increased frequency of drug product shortages has precipitated the development of nontraditional distributors, also known as open-market, gray-market, or alternative distributors. These specialty, licensed distributors or brokers obtain products in short supply for the purpose of reselling them to end users who are unable to obtain them through their normal suppliers. These distributors aggressively market the availability of these products to hospitals, specialty health systems, home care agencies, and physician practices, generally at substantially higher prices. Typically, these distributors have a limited quantity of product, often only enough for one or two patients. Many do not offer a return or refund on a product if it expires or is not used. Especially worrisome is the inability to ascertain the product's

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pedigree or ensure the reliability of the product's source, which could be outside the United States, and proper handling and storage throughout the chain of custody. The extent to which the activities of such nontraditional distributors contribute to drug product shortages is unknown.

Compounding pharmacies have also pursued the production of drugs that are in short supply. Caution is warranted because preparations from these pharmacies may not meet applicable state or federal standards (e.g., *United States Pharmacopeia* chapter 797 or FDA labeling requirements). The sources of raw materials used by compounding pharmacies have been questioned, and apparent lapses in quality control have resulted in serious patient injury, including death.¹³

Natural disasters. Natural disasters can have a profound effect on the availability of drug products. Damage to manufacturing facilities, particularly those that are the sole source of a drug product or category of products, is likely to cause long-term shortages. Damage to manufacturing facilities in Puerto Rico in 1998 from hurricane George caused shortages of several drug products. Fires, hurricanes, tornadoes, and floods are examples of natural disasters that may temporarily compromise drug product supplies. In some instances, these shortages may be exacerbated by an escalated need for certain classes of drug products to care for victims of the disaster. In 2005, areas affected by hurricanes Katrina and Rita were affected by both an increased need for medications and the inability to obtain them.

Phased approach to planning for drug product shortages

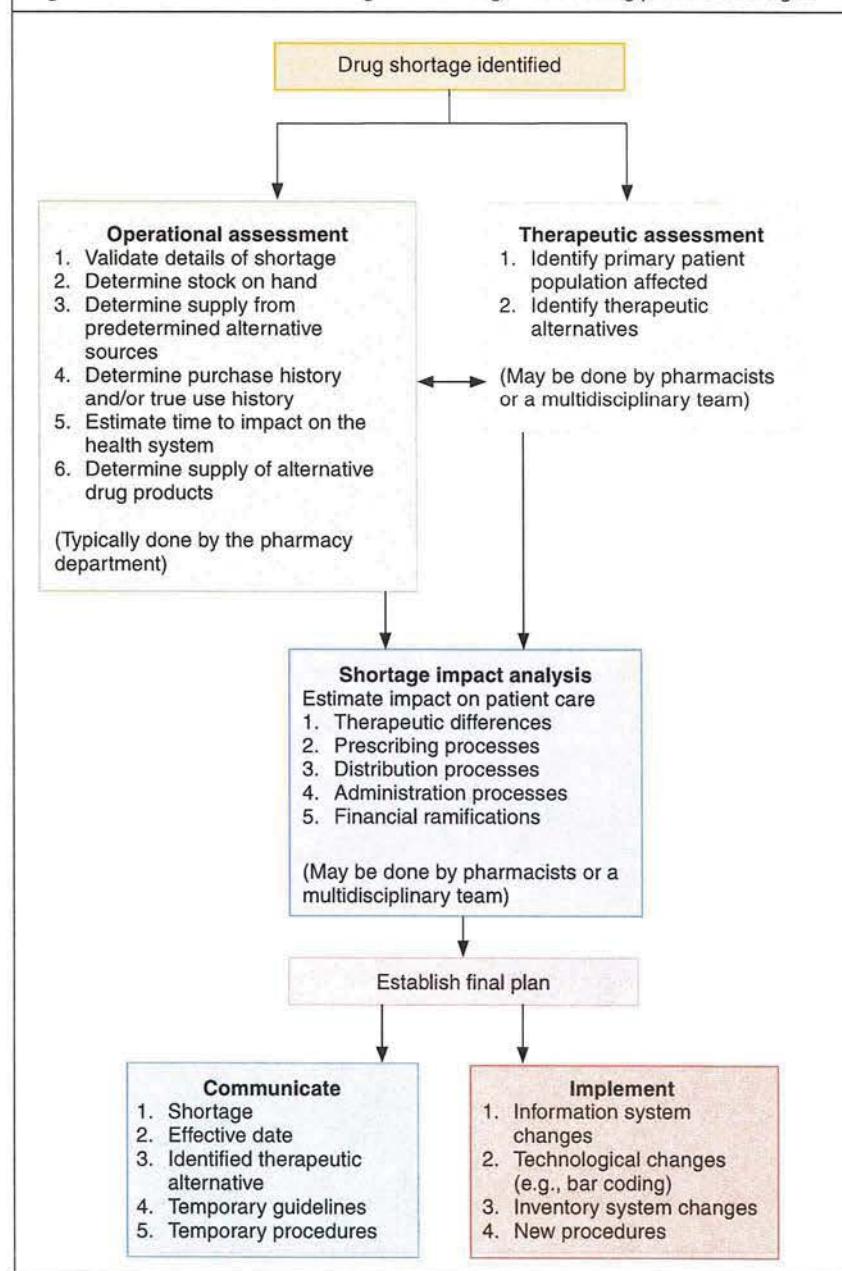
The discovery of a shortage initiates a cascade of events surrounding drug procurement and therapeutic decision-making (Figure 1). Drug procurement considerations include validating the shortage and its an-

ticipated duration, determining the availability of supplies from alternative sources, locating and procuring alternative supplies (if available), investigating the implications of compounding the product, and researching and providing education about alternative agents and the cost implications of all scenarios. The outcome of this process may prompt an eval-

ation of the shortage's potential effect on patient care and development of a strategy for effectively communicating the needed information to all professionals involved and to affected patients when warranted.

In an ideal world, there would be a system for warning providers in advance of impending drug product shortages; this would give them

Figure 1. Process for decision-making in the management of drug product shortages.



ample opportunity to proactively address and manage all aspects and implications of the shortage. In lieu of this ideal, pharmacists, when confronted with the unavailability of a drug product, want information on which to base decisions about meeting patient needs for the product. Segments of the supply chain, especially manufacturers and distributors, have been inconsistent in providing information and assistance to health systems. The difficulty in obtaining information is exacerbated by the many players, complexities, and uncertainties in the supply chain.

The pharmacy department must take a leadership role in managing shortages by developing and implementing appropriate strategies and processes for optimizing the safe and effective use of therapeutic alternatives. Health systems should develop a contingency planning strategy to prepare for the possibility of a prolonged drug product shortage.¹⁹ Although it often is not possible to predict when shortages will occur, the process for dealing with them can be defined in advance. The health system should identify a point person to implement and monitor this process and establish an organizational approach to decision-making and communication. The institution should determine committee structures and responsibilities for decision-making during each phase of the process (e.g., pharmacy and therapeutics committee, medical executive committee).

Planning can be divided into three phases: identification and assessment, preparation, and contingency. Assessment requires a critical evaluation of the current situation and the potential effect of the shortage on the health system. An effective evaluation examines the reason for the shortage and estimates an end date; both internal and external supply availabilities are assessed.

The preparation phase consists of all activities that can be performed

before the actual effects of the shortage are felt. Depending on the health system's inventory, when a back order or other notice is received, there is often lead-time before actual stock depletion. All patients whose treatment depends on the unavailable drug product and alternative therapies should be identified. Since many drug products have limited therapeutic alternatives, outages can have significant patient care and cost consequences. Health systems need to gauge the effect of those consequences on their institutions. Preparation should also include the development of methods for implementation and communication.

The contingency phase involves operations and circumstances for which preparation is limited because of incomplete information, financial constraints, or circumstances beyond the health system's control. For example, biological products are available only in increments and at a very high cost when no therapeutic alternatives are readily available or when shortages are longer than anticipated. Since direct control over availability is not possible, health systems must prepare for a product's unavailability.

Identification and assessment phase. The purchasing agent is often the person who identifies a shortage and may be the person responsible for managing drug product shortages. This person must be cognizant of aberrant fluctuations in the health system's supply chain that may indicate a potential shortage (e.g., partial orders filled, one strength difficult to obtain, most manufacturers have no more stock). If the purchasing agent is not a pharmacist, he or she must work with a designated pharmacist.

When a shortage is identified, the point person or his or her designee should conduct an assessment to evaluate its potential effect. A threat analysis using the shortage's expected duration and an assessment of the current inventory and usage patterns

can be used to determine the potential consequences of the shortage.

Details and duration of shortage. Pharmacists can contact product manufacturers, distributors, FDA, CDC, and other sources to determine the reason for the shortage and its expected duration. This information may already be available on the ASHP Drug Shortage Resource Center Web site (www.ashp.org/shortages). If not, visitors to the site can report a shortage online. Predictions of when the product will be available help determine the health system's ability to endure the shortage and guide its short- and long-term management strategies.

Although the end result is the same, the time to impact and the duration of effect vary according to the reason for the shortage and where in the supply chain problems occur—from raw materials to manufacturer, manufacturer to wholesaler, or wholesaler to health system. A lack of raw materials may affect several manufacturers of the finished drug product. A manufacturer's problems may affect only its product. Effects on distributors are dependent on their inventory levels.

Inventory on hand. Once a shortage is confirmed, the pharmacy should count the inventory on hand and estimate the time period it will cover. Available inventory includes all supplies of the drug product within the health system, including the pharmacies, inpatient units, ambulatory care clinics, automated medication storage and distribution devices, floor stock, resuscitation carts, and prepared trays.

Based on available quantities and historical usage, the pharmacy should estimate how long the health system can endure a shortage. Usage history can be obtained from procurement and issue records held by distributors, the purchasing department, and the pharmacy department. Billing and automated medication storage and dispensing device records can

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assist in determining actual usage within the system.

Inventory counts of all alternative drug products should be converted into common measurement units to augment estimates of use. Both current use rates and reduced rates after conservation measures are implemented should be included when assessing how long the available inventory of the shortage drug product and possible alternative products will last.

Threat to patient care and costs. A threat analysis evaluates all factors relevant to the shortage (e.g., duration, current inventory, medical necessity, alternative sources or therapies) to determine the shortage's potential effect on patient care and costs. Shortages affect safe medication practices throughout the medication distribution and administration process within a health system. When considering alternative dosage forms or therapies, pharmacists must consider changes in their procedures for look-alike and sound-alike medications, bar coding, distribution paths, and the effect on automation, contract compliance, and final product preparation.²⁰ The extent to which a health system will be affected by a given shortage depends on the health system's scope and level of services and its service population.

Preparation phase. Once an imminent shortage is confirmed, the health system should take steps to prepare for known and potential problems in maintaining patient care and controlling costs.

Therapeutic alternatives. The first step in the preparation phase is to identify therapeutic alternatives to the unavailable drug product. A formal process for identifying and approving therapeutic alternatives for the health system should be established. The health system should make decisions about alternative agents in collaboration with medical, nursing, and pharmacy representatives and obtain approval of the

appropriate medical committees. Therapeutic alternatives should be inventoried to ensure adequate supplies to meet new demand. In many cases, supplies of the best alternative agent may be affected by the current shortage.

Communication and patient safety. Information about the drug product shortage, alternative therapies, temporary therapeutic guidelines, and implementation plans should be communicated to clinical staff by the most effective means available within the health system. Communication of this information is essential for ensuring patient safety and preventing medication errors caused by confusion over differences between drug products' dosages, onsets, durations, and other factors. Automated systems and order-entry systems must be updated with changes. Pharmacy department staff responsible for assisting prescribers with medication orders and aiding nursing staff with administration should be thoroughly informed about the alternative therapy decisions and implementation plans. Sustained communication is necessary to reach medical, nursing, and pharmacy staffs working varied shifts or services.

External relationships with other health systems. The preparation phase includes, when applicable, the establishment of collaborative arrangements with other institutions within a regional network or system. Available supplies of a potentially unavailable product and information about alternative therapies should be shared among the facilities. This option is limited for rural hospitals and for area hospitals served by a single wholesaler.

Patient prioritization. When a limited supply of a drug remains available and alternatives for specific patient groups are undesirable, a health system may prioritize the drug for specific patient groups. National organizations (e.g., CDC, medical organizations) may provide guidance on

setting patient priorities. Medication-use evaluation data on prescribing and utilization trends, if available for the drug in question, may be useful in developing prioritization criteria to guide appropriate drug use. Such criteria are particularly helpful in dealing with long-term shortages such as with intravenous immunoglobulin. To limit product use for select patients or services in the health system, criteria should be developed by a multidisciplinary team. Communication is essential to ensure that adequate supplies are available to complete courses of therapy. Clear guidelines for prioritization must be provided to assist pharmacists in evaluating the appropriateness of medication orders.

Consultation with risk management and ethics staff members or committees may be useful when supplies are severely limited. For example, during the influenza vaccine shortage of 2004–05, many health systems did not have sufficient product to follow recommended CDC guidelines and further restricted use of the product to specific patient groups.

Stockpiling restraint. Inventory management is a challenge during a shortage. Despite pressure to do otherwise, stockpiling (hoarding) in advance of a feared shortage can occur; this can exacerbate the shortage and divert unneeded supplies away from other health systems with patients in need.²¹ Health systems should refrain from stockpiling, which causes two distinct problems:

1. Stockpiling can cause artificial shortages when health systems drain the supply chain and exceed manufacturing capacities, and
2. Increased inventory is costly and may not be absorbed by normal usage if shortages do not occur as anticipated.

Speculative purchasing in response to a potential shortage has drawbacks, depending on the likely

cause of the shortage and where it might occur in the supply chain. Problems may arise that pose threats to, but do not reach, end users. This happens when the supply chain, from raw material to finished product, contains several months' supply; the long lead-time allows corrections that avert a shortage.

During shortages, manufacturers and distributors often allocate a product on the basis of past usage. An initial stockpile order generally has no effect on increasing an allocation.

Contingency phase. Health systems must establish clear guidelines for dealing with situations in which a product is available only from a compounding source or nontraditional source or when a critical drug is not available at all.

Risk management and liability. One potential complication of a shortage is litigation by patients who feel that they have received improper care or suffered unanticipated adverse drug events as a result of delays, prioritization, alternative therapy, or nontraditional drug product sources. This situation is most likely with agents for which no alternatives are available. Even though risk management and legal representatives may have participated in earlier phases of the process, they should be notified immediately when all options for obtaining either the drug product or acceptable alternatives have been exhausted.

Each health system must determine its philosophy on purchasing drugs from the gray-market or compounding pharmacies and on compounding agents inhouse. These decisions should be made before the pressure and emotion of a specific shortage occur. Each option and its potential effect on patient risk should be evaluated. Nontraditional drug product sources (e.g., secondary wholesalers) have extremely limited supplies, and the quality of these products may be questionable, as the provenance of the medication

may be unknown. Compounding pharmacies may also present patient risks; several deaths have been associated with improperly sterilized compounded products.⁹ Health systems may choose to compound products if they can meet the necessary guidelines; however, obtaining raw materials may be difficult in some cases.

Budget considerations. In the event that the drug product is available only from noncontracted manufacturers or through nontraditional distributors, the increased costs of using these sources should be estimated. Using alternative therapies may also increase costs. The financial implications should be presented through budget channels, with a request and justification for contingency funds. Additional expenditures caused by drug product shortages (e.g., overtime spent in locating product, extra or priority deliveries, inhouse compounding or packaging) must be documented to explain budget variances and to support future budget proposals.

Information coordination and communication. Clear communication with all affected clinicians about the status of a shortage is vital. Some health systems may designate a specific department to manage communications; others may find that a collaborative strategy involving various organizational departments and committees works best. Patients or family members should be counseled when a drug product shortage will delay or compromise care, especially when patients have been stabilized on the drug product and when alternatives may not be as effective (e.g., pain or blood pressure medications). The Joint Commission requires that prescribers potentially affected by drug product shortages be actively alerted.¹⁰

Strategies for prevention

Communication with the media, national professional or patient organizations, and government agencies

can raise awareness of the shortage and its potential consequences. Notifying ASHP or FDA about a drug product shortage can initiate these efforts. Drawing attention to the shortage may encourage production by other manufacturers, collaborative efforts to develop alternative therapies, and ad hoc training opportunities on the safe and effective use of alternatives.

Government intervention

FDA is responsible for assisting with drug product shortages to the extent of its authority.¹¹ Its responsibilities are dispersed among several components of CDER. The extent of FDA's activities depends on whether a shortage meets "medical necessity" criteria. FDA will attempt to prevent or alleviate shortages of medically necessary products. A product is considered to be medically necessary or a medical necessity if it "is used to treat or prevent a serious disease or medical condition, and there is no other available source of that product or alternative drug that is judged by medical staff to be an adequate substitute."¹² Inconvenience to the patient and cost to the patient, institution, and manufacturer are insufficient reasons for classifying a product as a medical necessity.

A determination of medical necessity involves a risk-benefit evaluation of the compromising issue with the product versus the medical need. When FDA has determined that a shortage of a medically necessary product exists, the agency will act within its authority; actions may include discussions with pharmaceutical manufacturers to encourage additional sources, technical assistance to manufacturers experiencing cGMP difficulties, or expedited reviews of drug product marketing applications or cGMP-related improvements. FDA may take these actions whether the cause of the shortage involves business decisions to stop manufacturing the product, voluntary recalls, FDA

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enforcement actions, or other factors. Information on the availability of medically necessary drug products is posted on CDER's website, and information regarding the availability of blood and vaccine products regulated by FDA's Center for Biologics Evaluation and Research (CBER) is posted on CBER's website. FDA encourages consumers and health care professionals and organizations to report product shortages. Reports of drug product shortages can be made by e-mail via CDER's Drug Shortages website (www.fda.gov/cder/drug/shortages/default.htm), and reports on vaccine and blood product shortages via CBER's Biological Products Shortage website (www.fda.gov/cber/shortage/shortage.htm). FDA's shortage team will obtain information about availability and will work cooperatively with ASHP's drug product shortage team.

Conclusion

Drug product supply issues are becoming more frequent, whether they result from manufacturing difficulties or natural disasters that affect production, reductions in the supply of raw materials, voluntary recalls, manufacturer business decisions, FDA enforcement actions to ensure public safety, or stockpiling that leads to artificial shortages. Although it is impractical to prepare for every potential shortage, proper planning can minimize adverse effects on patient care and health-system costs

and prevent problems from escalating into crises. The key to success will undoubtedly be found in the effectiveness of information gathering, teamwork to assess options, and communication with providers, patients, and administrators.

References

1. U.S. Pharmacopeia Center for the Advancement of Patient Safety. Section I: USP medication error analysis; drug shortages affect patient safety. www.usp.org/pdf/EN/patientSafety/capsLink2004-10-01.pdf (accessed 2008 Sep 17).
2. Institute for Safe Medication Practices. Safety briefs: drug shortage causes error. www.bfr06.com/ISMP_12_3.pdf (accessed 2009 Mar 23).
3. Schwartz MA. Prescription drugs in short supply: case histories. New York: Marcel Dekker; 1980.
4. Provisional observations on drug product shortages: effects, causes, and potential solutions. *Am J Health-Syst Pharm.* 2002; 59:2173-82.
5. Fox ER, Tyler LS. Managing drug shortages: seven years' experience at one health system. *Am J Health-Syst Pharm.* 2003; 60: 245-53.
6. Baumer AM, Clark AM, Witmer DR et al. National survey of the impact of drug shortages in acute care hospitals. *Am J Health-Syst Pharm.* 2004; 61:2015-22.
7. Institute for Safe Medication Practices. National survey on drug shortages reveals high level of frustration, low regard for safety. www.ismp.org/Newsletters/acuteCare/articles/20010321_2.asp (accessed 2009 Mar 23).
8. Institute for Safe Medication Practices. Recent national shortage of fentanyl products presents potential problems when substituting sufentanil. *ISMP Med Saf Alert.* 2001; 6(Feb 7):1.
9. Traynor K. Meningitis deaths linked to drug shortages. www.ashp.org/import/news/HealthSystemPharmacyNews/newsarticle.aspx?id=648 (accessed 2008 Sep 17).
10. Element of performance 7, medication management standard 2.10 (selection and procurement). In: Comprehensive accreditation manual for hospitals. Oakbrook Terrace, IL: Joint Commission; 2007:MM-7.
11. Jensen V, Kimzey LM, Goldberger MJ. FDA's role in responding to drug shortages. *Am J Health-Syst Pharm.* 2002; 59:1423-5.
12. CDER manual of policies and procedures (MAPP) 6003.1: drug shortage management. Rockville, MD: Food and Drug Administration; 2006.
13. Rubin AJ, Gosselin PG. Shortages of drugs threaten patients. <http://articles.latimes.com/2001/may/06/news/mn-60196> (accessed 2009 Mar 23).
14. Szabo L. Shortages of pediatric cancer drugs are common. www.usatoday.com/news/health/2005-07-19-cancer-drugs_x.htm (accessed 2009 Mar 23).
15. Hensley S, Wysocki B. Shots in the dark. As industry profits elsewhere, U.S. lacks vaccines, antibiotics. *Wall St J.* 2005; Nov 8:A1.
16. Food and Drug Administration. Federal Food, Drug, and Cosmetic Act, Sec. 506C (21 U.S.C. 356c). Discontinuance of a life-saving product. www.fda.gov/opacom/laws/fdcact/fdcact5a3.htm#sec506c (accessed 2009 Mar 23).
17. Smith NM, Bresee JS, Shay DK et al. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2006; 55 (RR-10):1-42. [Erratum, *MMWR.* 2006; 55:800.]
18. FluZone (influenza vaccine) package insert. Swiftwater, PA: Sanofi Pasteur; 2006.
19. Schrand LM, Troester TS, Ballas ZK et al. Preparing for drug shortages: one teaching hospital's approach to the IVIG shortage. *Formulary.* 2001; 36:52,56-9.
20. Pick AM, Massoomi F, Neff WJ et al. A safety assessment tool for formulary candidates. *Am J Health-Syst Pharm.* 2006; 63:1269-72.
21. Myers CE. Artificial shortages of drug supplies. *Am J Health-Syst Pharm.* 1999; 56:727. Editorial.